PATENT COOPERATION TREA

10/540047

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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2328238 - 17/12/2004

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	14.12.2004
Applicant's or agent's file reference: PCT-152	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/ES 03/00666	29.12.2003	10.01.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68

Applicant
FUNDACION PARA LA INVESTIGACION CLINICA Y... et al

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 10.05.2005

Name and mailing address of the international preliminary examining authority:

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WRITTEN OPINION International application No. PCT/ES 03/00666

I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-17 as originally filed

Claims, Numbers

1-9 as originally filed

Drawings, Sheets

1/14-14/14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☒ furnished subsequently to this Authority in written form.
   ☒ furnished subsequently to this Authority in computer readable form.
   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-9: Yes
Inventive step (IS)	Claims	1-9: Yes
Industrial applicability (IA)	Claims	1-9: Yes

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:
   D1: CANCER RES. vol. 61, no. 24, 2001, pages 8654 - 8658
   D2: LUNG CANCER vol. 36, 2002, pages 15 - 16
   D3: CANCER RES. vol. 61, no. 4, February 2001, pages 1354 - 1357: cited in the application
   D4: LUNG CANCER vol. 38, no. 2, November 2002, pages 123 - 129
   D5: CANCER RES. vol. 62, September 2002, pages 4899 - 4902: cited in the application
   D6: WO 97 25442 A1

2. **Novelty (article 33(2) PCT):**
   Independent **claim 1** relates to an assay device for detecting the genetic predisposition to respond to treatment of antitumour drugs characterised by comprising at least one of the oligonucleotides selected from SEQ ID 1, 2, 5 and 6. Since none of the prior art **D1** (page 8654, last paragraph), **D2** (page 15, middle of the right-hand column), **D3** (page 1355, first paragraph), **D4** (page 124, middle of the right-hand column), **D5** (whole document) or **D6** (page 2, last paragraph) discloses any of these primers, independent **claim 1** is considered to be novel. The same conclusion applies to independent **claim 6** which relates to these oligonucleotides. Furthermore, the independent **claim 8** of the present application is also new since it relates to the use of the oligonucleotides of SEQ ID 3, 4, 7 or 8 for the detection of the genetic predisposition to treatment of antitumour drugs which are not disclosed in any of the cited prior art documents **D1-D6**.
   It is concluded that **claims 1-9** of the present application are novel and fulfil the requirements of **article 33(2) PCT**.

3. **Inventive merit (article 33(3) PCT):**
   D2 (passages see above), which can be considered to be the closest prior art, concerns the detection of the polymorphism Lys751Gln in patients suffering from lung cancer using the primers 5'-CCTCTGTTCTCTGCAGGAGGA-3' and 5'-CCTGCGATTAAAGGCTGTGGA-3'.
   The assay device of the present **claim 1** distinguishes itself from **D2** by the sequences involved in the assay device.
   The sequences used in the present **claim 1** being not structurally related to the

sequences disclosed in **D2**, the solution provided by the application to the problem of providing a new assay device for the detection of genetic predisposition to respond to treatment of antitumour drugs is considered as a non-obvious alternative to **D2**.
Therefore, **claims 1-5** are considered to involve an inventive merit.
The same reasoning applies to oligonucleotides of **claim 6**.
Similarly, the use **claim 8** involves also an inventive merit over the prior art since the use of such probes for the detection of the genetic predisposition is not suggested in the closest prior art.
It is concluded that **claims 1-9** of the present application involve an inventive merit and fulfil the requirements of **article 33(3) PCT**.

4. **Industrial applicability (Article 33(4) PCT):**
An industrial applicability of the invention is obvious and **claims 1-9** of the present application are considered to fulfil the requirements of **Article 33(4) PCT**.

5. From the wording of **claims 2 and 3** of the present application, it seems that these claims refer to the assay device of claim 1. Nevertheless, the dependency to claim 1 is not clearly stated, rendering the scope of claims 2 and 3 unclear (**article 6 PCT**).

6. Dependent **claim 4** introduces no further characterising feature to claim 1 because it only specifies the polymorphism to be detected by the assay device (**article 6 PCT**).
Similarly, dependent **claim 5** does not introduce any feature characterising the assay device because it defines the antitumour drug used for the treatment whereas the assay device is not characterised by the drug but by the sequences comprised in the device (**article 6 PCT**).

7. Dependent **claim 7** introduces a feature to specify the drug to which the predisposition to response is detected. This is not a characterising feature of the oligonucleotide primer of claim 6 from which claim 7 dependents (**article 6 PCT**).

8. In **claim 1**, the oligonucleotides of SEQ ID 1, 2, 5 and 6 are referred to as "probes" whereas in **claim 6** and in the description on pages 10 and 11, they are referred to as "primers" and *vice versa* for SEQ ID 3, 4, 7 and 8 of **claim 8**. An oligonucleotide is to be considered as a primer or a probe depending whether the oligonucleotide is extended or not. This discrepancy between the description and the claims renders the scope unclear (**article 6 PCT**).

9. Some of the literature documents are referred to twice in the description on pages 5-8

(see references 3 and 4, 5 and 6, 10 and 11 and 23 and 24) (**rule 5.1(a)(ii) PCT**).